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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/898,417	07/03/2001	Michael R. Rosen	65219-A/JPW/PJP	3315

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EXAMINER	
WHITEMAN, BRIAN A	

ART UNIT	PAPER NUMBER
1635	4

DATE MAILED: 01/30/2003

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/898,417	ROSEN ET AL.	
	Examiner	Art Unit	
	Brian Whiteman	1635	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *02 October 2002* .

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-31* is/are pending in the application.

4a) Of the above claim(s) *4-8,11,12 and 17-31* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-3,9,10,13-16* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☒ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *03 July 2001* is/are: a)☐ accepted or b)☒ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☒ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☒ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449) Paper No(s) *6* .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: .

DETAILED ACTION

Non-Final Rejection

Claims 1-31 are pending examination.

Applicant's election of Group VI (claims 1-3, 9-10, and 13-16 directed to a nucleic acid encoding MiRP1 and HCN1) in Paper No. 7 is acknowledged. Because applicant did not distinctly and specifically point out the supposed errors in the restriction requirement, the election has been treated as an election without traverse (MPEP § 818.03(a)).

Claims 4-8, 11-12, and 17-31 are withdrawn from further consideration pursuant to 37 CFR 1.142(b) as being drawn to a non-elected invention, there being no allowable generic or linking claim. Election was made **without** traverse in Paper No. 7.

Drawings

NOTE: In the next response, please submit a response to the PTO 948 because a PTO 948 is filed with this non-final rejection. If the reply to the Non-Final Rejection does not have a response to the PTO 948, the response will be considered non-responsive. See 37 CFR 1.85(a).

Specification

Applicant is reminded of the proper language and format for an abstract of the disclosure.

The abstract should be in narrative form and generally limited to a single paragraph on a separate sheet within the range of 50 to 150 words. It is important that the abstract not exceed 150 words in length since the space provided for the abstract on the computer tape used by the printer is limited. The form and legal phraseology often used in patent claims, such as "means" and "said," should be avoided. The abstract should describe the disclosure sufficiently to assist readers in deciding whether there is a need for consulting the full patent text for details.

The language should be clear and concise and should not repeat information given in the title. It should avoid using phrases which can be implied, such as, "The disclosure concerns," "The disclosure defined by this invention," "The disclosure describes," etc.

The abstract of the disclosure is objected to because the abstract is over 150 words and longer than 15 lines and for the phrase "a A vector" line 18. Correction is required. See MPEP § 608.01(b).

Claim Objections

Claim 14 is objected to because of the following informalities: recites topical administration twice in the claim. "Topical administration" is the same as "topical application to the cell". Suggest removing one of the phrases.

Claim 15 is objected to because of the following informalities: misspelling of the word "moyocytes" on line 3.

Claim 15 is objected to because of the following informalities: misspelling of the word "form" on line 5 should be "**from** step (a)".

Claim 15 is objected to because the steps are numbered (a,b,d) and not numbered in sequential order (a,b,c,d).

Claim 15 is objected to because of the following informalities: there is an unmatched parenthesis on line 2 step (b) after "(contacting a set of the cardiac myocytes form step (a) with an agent to be assayed for its effects on heart rate;". Appropriate correction is required.

Appropriate correction is required.

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 1-3, 9-10, and 13-16 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention.

The claimed invention embraces performing an assay on a heart that is either *ex vivo* or *in vivo*. The assay comprises: a) contacting a cardiac cell of a heart with an effective amount of a compound to cause a sustainable heart rate; b) measuring the heart rate after step a); c) providing the heart with an agent to be assayed for its affect on heart rate; d) measuring the heart rate after step c); and comparing the difference between step b) and step d), thereby determining whether the agent affects heart rate.

The specification provides working examples that will be briefly discussed herein: Action potential in isolated neonatal and adult rat ventricular myocytes was studied using adenoviral constructs comprising HCN1, HCN2, or HCN4. Example 1 produces an assay using an adenoviral construct to over-express a nucleic acid encoding HCN2 in rat ventricle cells that produces a pacemaker current comparable to the normal cardiac pacemaker in the sinus node (pages 35-37). The assay can be used as a high throughput rate assay for measuring agents that affect pacemaker current. Example 2 is directed to expressing HCN1 or HCN2 individually or with MiRP1 in Xenopus oocytes. Both HCN 1 and HCN2 express a small current when injected alone. Coexpression of HCN1 or HCN2 with minK results in similar current. However, a much larger current is observed when HCN1 or HCN 2 is coexpressed with MiRP1.

In view of the In Re Wands Factors, the as-filed specification does not provide sufficient guidance or factual evidence to make and use the claimed methods. The specification teaches measuring pacemaker current in isolated cardiac cells using transfection methods comprising contacting the isolated cardiac cells with a nucleic acid encoding HCN1, HCN2, or HCN4 or coexpressing HCN1 or HCN2 with MiRP1. However, the claims read on contacting a cardiac cell in a heart that is either *ex vivo* or *in vivo* and the as-filed specification does not provide sufficient guidance or factual evidence for using a heart in the claimed methods. The specification does not provide a working example of the claimed method. The as-filed specification does not provide sufficient guidance or factual evidence to reasonably correlate using isolated cardiac cells to making and using an assay using a heart that is either *ex vivo* or *in vivo*. One skilled in the art would understand that for the claimed methods to be enabled for using a heart; the heart would have to be fully functional and the specification lacks guidance for what method steps and materials are required for one skilled in the art to use (or maintain) a heart to practice the claimed methods. Furthermore, the claims read on an *ex vivo* or an *in vivo* method of measuring the heart rate and the as-filed specification does not provide sufficient guidance or factual evidence for measuring the heart rate of an isolated heart in the claimed methods. The state of the art is absent for teaching how to use a heart in an *ex vivo* or *in vivo* assay as set forth in the claims. The specification lacks guidance for what materials and methods are required for how to make and use the claimed assay methods comprising an *ex vivo* heart that display a heart beat. Thus, it would take one skilled in the art an undue amount of experimentation to practice the claimed methods because the specification does not provide the method steps and materials

required for using a heart that is either *ex vivo* or *in vivo* and/or measuring the heart rate of an isolated heart.

As a result, it is not apparent how one skilled in the art determines, without undue experimentation, which of the claimed methods are considered enabled, how is it apparent as to how one skilled in the art, without any undue experimentation, practices any method as contemplated by the claims, particularly given the unpredictability of making and using methods of assaying whether an agent affects heart rate using a heart that is either *ex vivo* or *in vivo* and/or the doubts expressed in the art of record.

In addition, with respect to claims 13 and 14, it is not apparent to one skilled in the art how to contact a cardiac cell of a heart that is either *ex vivo* or *in vivo* by co-culturing the heart with a nucleic acid. The specification teaches co-culturing cardiac cells with a nucleic acid *in vitro*. However, the specification and the art of record are absent for any method of co-culturing a heart that is either *ex vivo* or *in vivo* with a nucleic acid. Thus, the claimed embodiment is not enabled because of the lack of guidance provided by the specification to make and use the claimed methods.

In conclusion, the as-filed specification and claims coupled with the state of the art at the time the invention was made do not provide sufficient guidance and/or evidence to reasonably enable one skilled in the art to make and use any of the claimed methods. Given that using a heart that is either *ex vivo* or *in vivo* in an assay was unpredictable at the time the invention was made, and given the lack of sufficient guidance as to practice the methods cited in the claims, one skilled in the art would have to engage in a large quantity of experimentation in order to practice the claimed invention based on the applicant's disclosure.

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter, which the applicant regards as his invention.

Claims 13, 14, 15, and 16 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claim 13 recites the limitation "the nucleic acid" in lines 12 and 13 on page 73. There is insufficient antecedent basis for this limitation in the claim.

Claims 13 and 14 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for claiming an improper Markush group (See MPEP 2173.05(h)). The claims recite two distinct groups. One group is directed to routes of administration and the other group is directed products that can be used in a route of administration. The members of the group do not possess at least one property in common, which is mainly responsible for their function in the claimed relationship.

Claim 14 recites the limitation "administration of contacting" in line 14 page 73. There is insufficient antecedent basis for this limitation in the claim.

Claims 15 and 16 recite the limitation "step c)" in line 17, page 74. There is insufficient antecedent basis for this limitation in the claim.

Claims 15 and 16 are rejected under 35 U.S.C. 112, second paragraph, as being incomplete for omitting essential steps, such omission amounting to a gap between the steps. See MPEP § 2172.01. The omitted step is: step c).

NOTE: Claims 1-3, 9-10, and 13-16 from co-pending application 09/875,392 are the same as the claims 1-3, 9-10, 13-16 from the instant application. However, a statutory double patenting rejection cannot be made at this time since the claims elected in the instant application (claims 1-3, 9-10, 13-16) are drawn to a different invention than the elected claims (20-31) in '392. Should the non-elected claims be re-joined to the elected invention in either application then a statutory double patenting rejection will be made on the claims.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Brian Whiteman whose telephone number is (703) 305-0775. The examiner can normally be reached on Monday through Friday from 7:00 to 4:00 (Eastern Standard Time), with alternating Fridays off.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, John L. LeGuyader, SPE - Art Unit 1635, can be reached at (703) 308-0447.

Papers related to this application may be submitted to Group 1600 by facsimile transmission. Papers should be faxed to Group 1600 via the PTO Fax Center located in Crystal Mall 1. The faxing of such papers must conform with the notice published in the Official Gazette, 1096 OG 30 (November 15, 1989). The CM1 Fax Center number is (703) 308-4556.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is (703) 308-0196.

Scott D. Priebe

SCOTT D. PRIEBE, PH.D
PRIMARY EXAMINER

Brian Whiteman
Patent Examiner, Group 1635
1/24/03